PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT/US03/05730

To:
PAUL M. BOOTH
HELLER EHRMAN WHITE & MCAULIFFE LLP
1666 K STREET, N.W. SUITE 300
WASHINGTON, DC 20006-1228

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing (*day/month/year*)	03 AUG 2005

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
38509-0011	

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US03/05730	28 February 2003 (28.02.2003)	01 March 2002 (01.03.2002)

Applicant

UNIVERSITY OF UTAH RESEARCH FOUNDATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Cheyne D. Ly for Janice Ford Telephone No. 571-272-1600

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 38509-0011	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/05730	International filing date *(day/month/year)* 28 February 2003 (28.02.2003)	Priority date *(day/month/year)* 01 March 2002 (01.03.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C12Q 1/68; G06F 19/00 and US Cl.: 435/6; 702/27		
Applicant UNIVERSITY OF UTAH RESEARCH FOUNDATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15 September 2003 (15.09.2003)	11 July 2005 (11.07.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Cheyne D. Ly Telephone No. 571-272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/05730

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-27 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 28-32, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-5, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-13	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 9 and 12	YES
	Claims 1-8, 10, 11, and 13	NO
Industrial Applicability (IA)	Claims 1-13	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Claims 1-13 meet the criteria set out in PCT Article 33(2), because the prior art does not teach a method for identifying a set of genes as defined by steps (a)-(g) of claim 1, 3, or 5.

Claims 1-8,10, 11, and 13 lack an inventive step under PCT Article 33(3) as being obvious over Jeremy et al. (2001) in view of Geraci et al. (2001).

It is noted that the instant claims are examined only to the extent of the elected species of normal lung tissue in the search report.

Jeremy et al. discloses a method for identifying a set of genes from a multiplicity of genes (page 5227) wherein all experiments of hybridization are performed in triplicates (page 5224, column 1, lines 20-31) to identify differentially expressed genes in cell lines in a lung cancer model (Abstract etc.). Jeremy et al. discloses each of the four clusters (correlation) contained expression profiles of 61 (first), 67 (second), and 99 (third) genes (page 5225, column 1, lines 15-16), as instant claims 2, 8, and 10.

The genes are related to cell adhesion, motility, angiogenesis, and signal transduction (Abstract etc.), as in instant claims 1, 3, and 5, step (a).

Of the 9600 putative genes, 8525 had statistically significant expression value, and their expression profiles were grouped into 100 clusters (page 5225, column 1, lines 6-10), as in instant claims 1, 3, and 5, steps (b).

The SOM algorithm used by Jeremy et al. has been described by Tamayo et al. (page 5224, Statistical Analysis §). The inclusion of the reference by Tamayo et al. is to expand on the inherent characteristics of said SOM algorithm. SOMs are constructed by iteratively selecting a data point P and moving the nodes in the direction of P to defined related clusters (optimal). Nodes are iteratively mapped onto k-dimensional "gene expression space" (locally). The process continues for 20,000-50,000 iterations (Tamayo et al., page 2908, column 1, SOMs §), as in instant claims 1, 3, and 5, steps (c)-(g).

The method of Jeremy et al. is directed to human lung adenocarcinoma cell lines (page 5223, column 2, Cell Lines §), as in instant claim 7.

Tamayo et al. discloses SOM mapping is based on a formula (parametric function) defined on page 2908, column 2, as in instant claim 11.

The method of Jeremy et al. is based on spotted cDNA sequences (page 5224, column 1, lines 20-31), as in instant claim 13.

Jeremy et al. discloses an improvement for identifying multiple genes that orchestrate the process of lung cancer metastasis by differential gene expression (Abstract etc.).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

However, Jeremy et al. does not disclose the limitation of normal lung tissue.

Geraci et al. discloses a method for characterizing normal lung tissue comprising cells by differential gene expression patterns (Abstract etc. and Figure 2), as in instant claims 4 and 6.

An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Jeremy et al. and apply said improvement to the method of characterizing normal lung tissue by differential gene expression patterns as taught by Geraci et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the method of identifying multiple genes in normal lung tissues by differential gene expression patterns as taught by Jeremy et al. and Geraci et al.

Claims 9 and 12 meet the criteria set out in PCT Article 33(3), because the prior art does not teach or fairly suggest a method for identifying a set of genes comprising the limitation of third predetermined number is 1%, 5% or Mahalanobis distance.

Claims 1-13 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in the biotechnology industry.

Tamayo et al., Proceedings of National Academy of Science, U S A. 1999 March 16; 96 (6): 2907-2912.
Geraci et al., Circulation Research, 2001 Mar 30; 88(6):555-562.